REMARKS

Any fees that are due with this paper or application can be charged to Deposit Account No. 50-1213. If a Petition for extension of time is due, this paper can be considered such Petition.

Claims 1-21 are presently pending in this application. Claim 1 is amended to more distinctly claim the subject matter by including as an element a free 3' hydroxyl at the 3' end, which by definition is required for the 3' end to be capable of being extended by an enzyme to generate an extension segment as claimed (for example, see Lewin, *Genes*, page 680 (1983)). Claim 19 is amended for clarity. Therefore, no new matter is added nor are any amendments made to change the scope of the claims. The amendment should place the claims and the application into condition for allowance.

THE REJECTION OF CLAIMS 1-15 and 18-20 UNDER 35 U.S.C. §102(e)

Claims 1-15 and 18-20 are rejected under 35 U.S.C. § 102(e) as anticipated by Hiatt *et al.* (U.S. Patent 5,763,594) because Hiatt *et al.* allegedly discloses a nucleic acid primer having a first region containing the 5' end of the primer and an immobilization attachment site, and a second region containing the 3' end of the primer and a selectively chemically cleavable site, where the 3' end is capable of being extended by an enzyme to generate an extension segment. It is further alleged that Hiatt *et al.* discloses the limitations of dependent claims 2-15 and 18-20. The Examiner alleges that the 3' blocking moiety of Hiatt *et al.* in the second region is the selectively chemically cleavable site. The Examiner further states that Hiatt *et al.* does not "explicitly disclose that a second region contains a selectively chemically cleavable [site]" but alleges that "chemically cleavable is always selective."

This rejection is respectfully traversed.

RELEVANT LAW

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. *In re Spada*, 15 USPQ2d 1655 (Fed. Cir. 1990); *In re Bond*, 15 USPQ 1566 (Fed. Cir. 1990); *Soundscriber Corp. v.*

U.S., 360 F.2d 954, 148 USPQ 298, 301, adopted 149 USPQ 640 (Ct. Cl. 1966). See, also, *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir.), *cert. denied*, 110 S.Ct. 154 (1989). "[A]ll limitations in the claims must be found in the reference, since the claims measure the invention". *In re Lang*, 644 F.2d 856, 862, 209 USPQ 288, 293 (CCPA 1981). Moreover, it is incumbent on the Examiner to identify where each and every facet of the claimed invention is disclosed in the reference. *Lindemann Maschinen-fabrik Gmbh v. American Hoist and Derrick Co.*, 730 F.2d 1452, 221 USPQ 481 (Fed. Cir. 1984). Further, the reference must describe the invention as claimed sufficiently to have placed a person of ordinary skill in the art in possession of the invention. *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981).

THE CLAIMS

Independent claim 1 and its dependent claims (2-21) are directed to a nucleic acid primer having a 5′ end and a 3′ end, which includes a first region containing the 5′ end of the primer and an immobilization attachment site; and a second region containing the 3′ end of the primer having a free 3′ hydroxyl and a selectively chemically cleavable site. The 3′ end is capable of being extended by an enzyme to generate an extension segment. When the primer is immobilized via the immobilization attachment site, and the selectively chemically cleavable site is cleaved, the remainder of the primer remains immobilized.

Differences Between the Claims and the Teachings of the Cited Reference

Hiatt *et al.* (5,763,594)

Hiatt *et al.* discloses a method for the synthesis of a polynucleotide of a predetermined sequence where the 3′-hydroxyl group of a deoxynucleotide triphosphate can be protected and deprotected for use by a template-independent polymerase to extend the initiating substrate a predetermined sequence (col. 4, lines 5-15). Hiatt *et al.* discloses removable blocking groups, including carbonitriles, phosphates, carbonates, carbamates, esters, ethers,

borates, sugars, phosphoramidates and others that block the 3' position and when removed produce a hydroxyl group at the 3' position (col. 4, lines 59-67 and col. 10, lines 21-62).

ANALYSIS

Hiatt *et al.* does not anticipate any of the instant claims, because Hiatt *et al.* does not disclose primers with a 3' end that includes a free 3' hydroxyl and a *selectively chemically* cleavable site.

The Examiner appears to allege that the blocking group at the 3' end of the nucleotides of Hiatt *et al.* are equivalent to the instantly claimed *selectively chemically* cleavable site. Applicant respectfully submits that if the oligonucleotide of Hiatt *et al.* contains a 3' blocking group and thus the "selectively chemically cleavable site" alleged by the Examiner, then the oligonucleotide does not have a free 3' hydroxyl group as required in the instant claims. Hiatt *et al.* discloses that its blocking group eliminates the free 3' hydroxyl group of the oligonucleotide, and it is only by removing the blocking group that a free hydroxyl group at the 3' position is produced (see col. 4, lines 59-64). If the blocking group is removed, then the oligonucleotide would have a free 3' hydroxyl that be available for use as a primer, but then the alleged "selectively chemically cleavable site" is not present at the 3' end.

The instant claims require both limitations - the oligonucleotides be primers with a free 3' hydroxyl AND a selectively chemically cleavable site at the 3' end. The oligonucleotides of Hiatt *et al.* have **EITHER** protecting groups (the alleged "selectively chemically cleavable site") and no free 3' hydroxyl group **OR** they are deprotected and have a free 3' hydroxyl group but no "selectively chemically cleavable site". They do NOT have both.

Thus, Hiatt *et al.* does ***not*** disclose a nucleic acid primer having a second region at the 3' portion that includes a free 3' hydroxyl and a selectively chemically cleavable site. Therefore, the cited reference fails to disclose every element of the claimed subject matter. Accordingly, Hiatt *et al.* does not anticipate any of claims 1-21.

REJECTION OF CLAIMS 16 AND 17 UNDER 35 U.S.C. §103(a)

Claims 16 and 17 are rejected under 35 U.S.C. §103(a) as being unpatentable over Hiatt *et al.* in view of Edwards *et al.* (US 5,547,835) because Hiatt *et al.* allegedly teaches all elements of the claims except for a solid support that includes an antibody or an anti-digoxigenin antibody, and Edwards *et al.* allegedly cures this defect. This rejection is respectfully traversed.

RELEVANT LAW

In order to set forth a *prima facie* case of obviousness under 35 U.S.C. §103: (1) there must be some teaching, suggestion or incentive supporting the combination of cited references to produce the claimed invention (*ACS Hospital Systems, Inc. v. Montefiore Hospital*, 732 F.2d 1572, 1577, 221 USPQ 329, 933 (Fed. Cir. 1984)) and (2) the combination of the cited references must actually teach or suggest the claimed invention. Further, that which is within the capabilities of one skilled in the art is not synonymous with that which is obvious. *Ex parte Gerlach*, 212 USPQ 471 (Bd. APP. 1980). Obviousness is tested by "what the combined teachings of the references would suggest to those of ordinary skill in the art" *In re Keller*, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981), but it cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination (*ACS Hosp. Systems, Inc. v Montefiore Hosp*. 732 F.2d 1572, 1577, 221 USPQ 329, 933 (Fed. Cir. 1984)).

"To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher" *W.L. Gore & Associates, Inc. v. Garlock Inc.*, 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983).

THE CLAIMS

Claim 16 depends from claim 11 and is directed to an embodiment where the primer includes as a solid support an antibody.

Claim 17 depends from claim 16 and is directed to an embodiment where the antibody includes anti-digoxigenin.

Differences Between the Claims and the Teachings of the Cited References

Hiatt *et al.*

See related section above.

Edwards *et al.*

Edwards *et al.* teaches a DNA:protein binding assay for screening libraries of synthetic or biological compounds for their ability to bind to a selected test sequence in a duplex DNA (col. 2, lines 58-62). The target oligonucleotide is labelled to allow detection (col. 4, lines 35-36). The label can be radiolabels or digoxigenin (col. 4, lines 36-41). In one embodiment, the target site includes digoxigenin as a label and a biotin moiety to interact with streptavidin attached to a solid support, and the target is detected using a tagged anti-digoxigenin antibody (col. 4, lines 44-50). In another embodiment, the target site includes biotin as a label and digoxigenin to interact with anti-digoxigenin antibody attached to a solid support, and the target is detected using tagged streptavidin (col. 4, lines 51-56).

ANALYSIS

It is respectfully submitted that the Examiner has failed to set forth a case of *prima facie* obviousness for the following reasons.

The combination of teachings of Hiatt *et al.* with the teachings of Edwards *et al.* does not result in the instantly claimed primers.

As discussed above, Hiatt *et al.* does not teach or suggest a nucleic acid primer that includes a second region containing the 3' end of the primer that includes a free 3' hydroxyl and a selectively chemically cleavable site, and Edwards *et al.* does not cure this defect. Edwards *et al.* does not teach or suggest a nucleic acid primer having a 5' end and a 3' end that includes a first region containing the 5' end and an immobilization attachment site; and a second region containing the 3' end that includes a free 3' hydroxyl and a selectively chemically cleavable site. Edwards *et al.* does not teach or suggest that the 3' end of its nucleic acid is capable of being extended by an enzyme to

generate an extension segment. Edwards *et al.* does not teach or suggest a nucleic acid that includes a selectively chemically cleavable site immobilized to a solid support by an immobilization attachment site where, when the selectively chemically cleavable site is cleaved, the remainder of the primer remains immobilized.

Thus, even if, arguendo, Edwards *et al.* teaches a DNA:protein binding assay where the target oligonucleotide is attached to the solid support using an anti-digoxigenin antibody that is attached to the solid support, combining the teachings of Hiatt *et al.* and Edwards *et al.* does not result in the subject matter of claims 16 and 17. Therefore, because the combination of teachings of Hiatt *et al.* and Edwards *et al.* does not result in the instantly claimed subject matter, the Examiner has failed to set forth a *prima facie* case of obviousness.

REJECTION OF CLAIM 21 UNDER 35 U.S.C. §103(a)

Claim 21 is rejected under 35 U.S.C. §103(a) as being unpatentable over Hiatt *et al.* in view of Köster (US 5,547,835) because Hiatt *et al.* allegedly teaches all elements of the claim except using the single-stranded nucleic acid complementary to an intermediary oligonucleotide that is bound to a solid support, and Köster allegedly cures this defect.

This rejection is respectfully traversed.

RELEVANT LAW

See related section above.

CLAIM 21

Claim 21 ultimately depends from claim 1 and is directed to an embodiment thereof that includes a solid support, where the single stranded nucleic acid is complementary to an intermediary oligonucleotide bound to the solid support and where the primer is attached to the solid support by hybridization of the immobilization attachment site to the intermediary oligonucleotide.

Differences Between the Claims and the Teachings of the Cited References

Hiatt *et al.*

See related section above.

Köster

Köster teaches a mass spectrometric method for sequencing using a Sanger sequencing strategy, in which one embodiment includes immobilizing the sequencing primers to a support using various linkers. Köster teaches that the primer has a linking functionality L at the 5'-end that interacts with a suitable functionality L' on the solid support to form a reversible linkage L–L', cleavage of which removes the entire primer from the solid support (column 11, line 52 - column 13, line 2).

ANALYSIS

It is respectfully submitted that the Examiner has failed to set forth a case of *prima facie* obviousness for the following reasons.

The combination of teachings of Hiatt *et al.* with the teachings of Köster does not result in the instantly claimed primers.

As discussed above, Hiatt *et al.* does not teach or suggest a nucleic acid primer that includes a second region containing the 3' end of the primer that includes a free 3' hydroxyl and a selectively chemically cleavable site, and Köster does not cure this defect.

Köster does not teach or suggest a nucleic acid primer that includes at the 3' end a free 3' hydroxyl and a selectively chemically cleavable site, such that when the primer is immobilized, and the selectively chemically cleavable site is cleaved, the remainder of the primer remains immobilized. Thus, Köster fails to cure the deficiencies in the teachings of Hiatt *et al.* The combination of teachings of Hiatt *et al.* and Köster does not teach or suggest a nucleic acid primer having a 5' end and a 3' end, where the 3' end of the primer includes a free 3' hydroxy and a selectively chemically cleavable site. Thus, even if, arguendo, Köster teaches capturing oligonucleotides to a solid support via a complementary single-stranded nucleic acid, combining the teachings of Hiatt *et al.* and Köster does not result in the subject matter claimed in claim 21.

Therefore, the Office Action does not set forth a *prima facie* case of obviousness, and the rejection should be withdrawn.

* * *

In view of the amendments and remarks herein, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,
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